General

Guideline Title

Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.

Bibliographic Source(s)

Ramnath N, Dilling TJ, Harris LJ, Kim AW, Michaud GC, Balekian AA, Diekemper R, Detterbeck FC, Arenberg DA. Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e314S-40S. [132 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Robinson LA, Ruckdeschel JC, Wagner H Jr, Stevens CW, American College of Chest Physicians. Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):243S-65S.

Jett JR, Schild SE, Keith RL, Kesler KA, American College of Chest Physicians. Treatment of non-small cell lung cancer, stage IIIB: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):266S-76S.

Recommendations

Major Recommendations

The grades of recommendation (1A–2C) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

Infiltrative Stage III (N2/N3) Disease

In patients with infiltrative stage III (N2,3) non-small cell lung cancer (NSCLC) and performance status 0–1 being considered for curative-intent treatment, radiotherapy alone is not recommended (Grade 1A).

In patients with infiltrative stage III (N2,3) NSCLC and performance status 0–1 being considered for curative-intent treatment, combination platinum-based chemotherapy and radiotherapy (60–66 Gy) are recommended (Grade 1A).

Remark: Dose escalation of radiotherapy is not recommended (except in a clinical trial).

Remark: For patients with stage IIIB NSCLC, once daily thoracic radiotherapy plus platinum-based doublet chemotherapy is recommended.

In patients with infiltrative stage III (N2,3) NSCLC, performance status 0–1, and minimal weight loss being considered for curative-intent treatment, concurrent chemoradiotherapy is recommended over sequential chemoradiotherapy (Grade 1A).

Remark: The authors cannot currently recommend for or against induction chemotherapy (i.e., before) concurrent chemoradiotherapy, and patients should be referred for clinical trials to answer this question.

Remark: The authors cannot currently recommend for or against consolidation chemotherapy (i.e., after) concurrent chemoradiotherapy, and patients should be referred to clinical trials to answer this question.

In patients with infiltrative stage III (N2,3) NSCLC with a complete response after treatment with concurrent chemoradiotherapy, it is suggested that prophylactic cranial irradiation (PCI) should not be given (outside of a clinical trial) (Grade 2C).

In patients with infiltrative stage III (N2,3) NSCLC and performance status 0–1 being considered for curative-intent treatment, treatment with neoadjuvant (induction) chemotherapy or chemoradiotherapy followed by surgery is not recommended (Grade 1C).

In patients with infiltrative stage III (N2,3) NSCLC and performance status 2 or those with substantial weight loss (>10%), concurrent chemoradiotherapy is suggested but with careful consideration of the potential risks and benefits (Grade 2C).

Remark: Patient-related and tumor-related factors can influence the balance of risks vs benefits; patient preferences should also play a significant role.

In patients with infiltrative stage III (N2,3) NSCLC, performance status 0–1, and minimal weight loss being considered for curative-intent treatment, a platinum-based doublet chemotherapy is suggested (Grade 2C).

Remark: An optimal agent to be combined with platinum cannot be defined; one should choose a regimen with an acceptable toxicity profile for the individual patient among several combinations that have demonstrated activity when used concurrently with radiation in stage III NSCLC.

In patients with symptomatic infiltrative stage III (N2,3) NSCLC and either performance status 3–4, comorbidities, or disease too extensive to treat with curative intent, palliative radiotherapy is recommended. The fractionation pattern should be chosen based on the physician's judgment and patient's needs (Grade 1C).

Discrete Mediastinal Node Involvement

In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA), it is recommended that the treatment plan should be made with the input from a multidisciplinary team (Grade 1C).

Remark: The multidisciplinary team should include at a minimum a thoracic surgeon, medical oncologist, and radiation oncologist.

Remark: The decision should be made collaboratively by the entire team so as to reflect collective judgment.

Remark: The plan should include the entire proposed treatment, including plans contingent on the results of reevaluations (i.e., initial treatment response or nonresponse), not simply a first step.

In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA), either definitive chemoradiation therapy or induction therapy followed by surgery is recommended over either surgery or radiation alone (Grade 1A).

Remark: As the data do not permit the selection of one option or the other as superior, patient values and preferences should factor significantly in the decision.

Remark: All multimodality therapy should be performed in centers with experienced multidisciplinary teams that track their relevant clinical outcomes and are capable of minimizing and managing the toxicity and complications involved.

Remark: Further identification of patients more likely to benefit from surgical resection after induction therapy is not possible based upon pretreatment characteristics. Decisions to pursue surgical resection after induction therapy should be made prior to initiation of any therapy.

In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA), primary surgical resection followed by adjuvant therapy is not recommended (except as part of a clinical trial) (Grade 1C).

Occult N2 Involvement Despite Thorough Preoperative Staging (Stage IIIA)

In patients with NSCLC undergoing surgical resection, systematic mediastinal lymph node sampling or complete mediastinal lymph node dissection (MLND) is recommended (Grade 1B).

Remark: At least a systematic sampling is needed to accurately assess the pathologic stage; this is critical to direct adjuvant therapy.

Remark: It is unclear whether lymphadenectomy offers a survival benefit over systematic sampling, but in general, lymphadenectomy is suggested if there is evidence of N2 node involvement.

In patients with NSCLC who have incidental (occult) N2 disease (IIIA) found at surgical resection despite thorough preoperative staging and in whom complete resection of the lymph nodes and primary tumor is technically possible, completion of the planned lung resection and mediastinal lymphadenectomy is suggested (Grade 2C).

Remark: This recommendation assumes that staging for distant disease and invasive preoperative mediastinal staging according to guidelines have been carried out.

Remark: In a patient who has not received preoperative staging despite clinical suspicion of N2 node involvement (i.e., enlarged on computed tomography [CT], uptake on positron emission tomography [PET], or negative CT and PET but with a central tumor or N1 involvement), the operation should be aborted and staging completed if N2 disease is identified intraoperatively.

In patients with resected NSCLC (R0) who were found to have incidental (occult) N2 disease (IIIA) despite thorough preoperative staging and who have good performance status, adjuvant platinum-based chemotherapy is recommended (Grade 1A).

Remark: The authors suggest this should typically involve a doublet regimen for 3–4 cycles initiated within 12 weeks.

In patients with R0 resected NSCLC who were found to have incidental (occult) N2 disease (IIIA) despite thorough preoperative staging, sequential adjuvant radiotherapy is suggested when concern for a local recurrence is high (Grade 2C).

Remark: Adjuvant postoperative radiotherapy (PORT) reduces the incidence of local recurrence, but it is unclear whether it improves survival.

Remark: Adjuvant chemotherapy should be used initially followed by radiotherapy; concurrent chemoradiotherapy is not recommended (except in a clinical trial).

In patients with NSCLC who were found to have incidental (occult) N2 disease (IIIA) despite thorough preoperative staging and were incompletely resected (R1,2), combined postoperative concurrent chemotherapy and radiotherapy is suggested (Grade 2C).

Remark: Incomplete resection (R1,2) does not appear to confer a survival benefit over no resection.

Definitions:

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation, low- or very-low-quality evidence, Grade 1C	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Weak recommendation, moderate-quality evidence, Grade 2B	Benefits closely balanced with risks and burden	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Stage III non-small cell lung cancer (NSCLC)

Guideline Category

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Oncology

Pulmonary Medicine

Radiation Oncology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

- To inform the clinical decisions that must be jointly made by physicians and patients in developing diagnostic, treatment, and management plans so that they can enhance the benefits and reduce the harms associated with various options
- To update the published clinical trials since the last American College of Chest Physicians (ACCP) guidelines to make treatment recommendations for this controversial subset of patients.

Target Population

Patients with stage III non-small cell lung cancer (NSCLC)

Interventions and Practices Considered

1. Infiltrative stage III (N2,3) non-small cell lung cancer (NSCLC)
    - Combination platinum-based chemotherapy and radiotherapy (60–66 Gy)
    - Dose escalation of radiotherapy (only as part of a clinical trial)
    - Once-daily thoracic radiotherapy plus platinum-based doublet chemotherapy
    - Prophylactic cranial irradiation (PCI) (only as part of a clinical trial)
    - Platinum-based doublet chemotherapy
    - Palliative radiotherapy
2. Discrete mediastinal node involvement
    - Multidisciplinary team evaluation
    - Either definitive chemoradiation therapy or induction therapy followed by surgery
    - Primary surgical resection followed by adjuvant therapy (only as part of a clinical trial)
3. Occult N2 involvement despite thorough preoperative staging (stage IIIA)
    - Systematic mediastinal lymph node sampling or complete mediastinal lymph node dissection (MLND)
    - Lymphadenectomy or lung resection (after staging)
    - Adjuvant platinum-based chemotherapy
    - Concurrent chemoradiotherapy (only as part of a clinical trial)
    - Combined postoperative concurrent chemotherapy and radiotherapy

Major Outcomes Considered

- Outcomes of primary surgery vs preoperative (induction or neoadjuvant) therapy followed by surgery
- Recurrence rate

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To update previously published guidelines for the treatment of stage III non-small cell lung cancer (NSCLC), the writing committee repeated prior searches of MEDLINE for studies of therapy for stage III NSCLC as well as performed new systematic searches of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews up to December 2011, including primarily randomized trials, selected meta-analyses, practice guidelines, and reviews. In addition, the panel identified additional articles by searching personal files and reviewing reference lists of included studies. The committee formulated key population, intervention, comparison, and outcome (PICO) questions (see Table S1 [see the "Availability of Companion Documents" field]).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Assessment of Study Quality

Systematic reviews and meta-analyses were assessed using Documentation and Appraisal Review Tool (DART) (R. L. Diekemper; B. K. Ireland, MD; and L. R. Merz, PhD, MPH, DART, unpublished data, 2012), which was developed as an improved alternative to the existing tools for use in a clinical setting. However, this tool has been adopted for use in American College of Chest Physicians (ACCP) guidelines and consensus statements since 2011.

Quality was assessed for each study as well as for the body of relevant evidence. Based on the population, intervention, comparator, and outcome (PICO) questions and volume of available literature, multiple study designs were included in the systematic reviews of the literature. Randomized controlled trials (RCTs) primarily indicate benefits, but whenever observational studies met inclusion criteria they were often helpful in identifying harms. Observational studies were also examined when RCTs were not available to answer a particular PICO question. Allowing for multiple study designs resulted in the need for multiple quality assessment tools. Tools were chosen for assessing RCTs, observational studies, and diagnostic studies. The quality assessment tool for RCTs (R. L. Diekemper, B. K. Ireland, and L. R. Merz, unpublished data, 2012) was used for assessing the quality of RCTs, and a tool developed by the committee of the ninth edition of the Antithrombotics Guidelines was used for assessing the quality of observational studies. Diagnostic studies were assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS).

Meta-analyses

If a recently published good-quality meta-analysis was available, then it was used to inform the recommendations. When a good-quality meta-analysis was not available, guideline authors were encouraged to perform their own meta-analyses. Meta-analyses were performed when the data were fairly homogeneous. If a study was deemed poor quality, then it was not included in the pooled analysis. Heterogeneity of the pooled results was assessed using a χ^2 test and Higgins I^2, and a forest plot was examined for consistency of the results. The random effects model was chosen a priori as the appropriate model for pooling the data because it accounts for heterogeneity among the included studies. Results from the meta-

analyses are available in the supplementary materials that can be downloaded from the Journal website under the corresponding article in the table of contents.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition and Responsibilities

A call for applications to serve on the 3rd edition of the American College of Chest Physicians (ACCP) Lung Cancer Guidelines (LC III) panel was put forth to the ACCP membership, to past panelists, and to other organizations that have previously endorsed earlier editions of these guidelines or appointed representatives to serve on those panels. Guiding the team was the LC III Executive Committee, composed of a Panel Chair, Vice Chair, Liaison to the Guidelines Oversight Committee (GOC), and two staff members, one serving as an adviser and the other as the lead methodologist. The GOC appointed the Liaison and the Chair, who was required to be free of conflicts of interest (COI). This Executive Committee provided general oversight and guidance; multiple reviews of research questions, article outlines, manuscripts, evidence tables, and other supporting documents; and facilitation of the final conference discussions and voting. As the scope was defined, content experts in each major area were identified to serve as topic editors and nominated by the Panel Chair to be advanced to the GOC for the requisite qualifications and COI review and approval process. These topic editors organized their research and writing teams, oversaw the work of the individual members, edited separate contributions into synthesized manuscripts, presented evidence at the final conference, and managed any of their committee members who were approved with management stipulations relevant to their COIs.

Each topic editor was initially charged with proposing individuals to support their topic committees with expertise in the content area and/or methodology. With the Chair's approval, these individuals were nominated for GOC reviews for COI and expertise. In some cases, GOC staff helped to locate additional methodologic support when it was determined to be necessary for various article committees. This resulted in an international panel of >100 multidisciplinary experts across 24 articles representing the fields of pulmonary medicine, critical care medicine, thoracic surgery, medical and radiation oncology, pathology, integrative medicine, primary care, health-care research, guidelines methodology, and epidemiology. Nineteen international organizations that are also dedicated to advancing research and practice in the area of lung cancer were invited to appoint representatives to this guideline project as adjunct participants. These individuals, unless already approved panelists, were not considered full voting members of the panel, since they had not been through the same ACCP COI review, but were included at the final conference, participated fully in the discussions, and provided external review and feedback on the manuscripts and supporting documentation.

Formulating the Recommendations

In most cases the topic editors, along with the other completely non-conflicted members of the article committee, formulated the recommendations. The summarized evidence tables and profiles (where profiles existed) provided the foundation for the recommendations. In formulating the recommendations, panelists considered not only the body of evidence but also the balance between the benefits and harms and considerations of other factors, such as cost or resource availability considerations and patient values and preferences, which might vary widely for some recommendations. These additional considerations are described in a Remarks section, which appears just below the relevant recommendation in the publication, each time the recommendation appears.

Grading the Recommendations

Recommendations that are strong must be differentiated from those that are weak or weaker. Thus, the ACCP Grading System was used (see the "Rating Scheme for the Strength of the Recommendations" field), and the wording of the recommendations is explicit. This grading system has been used since 2005 and is based on two dimensions: the balance of benefits to harms and the quality of the evidence base. If the benefits clearly outweigh the harms or the harms clearly outweigh the benefits, the strength of the recommendation is considered strong and graded as a 1. In most cases, when there is strong confidence that the benefits outweigh the harms, most patients would choose the intervention endorsed in that recommendation. However, when the tradeoffs between desirable and undesirable consequences are not as clear, variability in patient preferences and values often becomes germane to the decision-making conversation.

Weak recommendations are those for which the benefits and harms are more equally balanced, and thus a clear choice is not as obvious; these are graded with a 2. Strong recommendations are phrased, "the panel recommends," whereas weak recommendations are phrased "the panel suggests." Accompanying these indications of the strength of a recommendation is a letter score (A, B, or C) representing the grading of the body of relevant literature.

In grading the quality of the evidence, RCTs start with a high score but might be downgraded to moderate or even low based on the following criteria: limitations in the study design or conduct of the trial, imprecision, indirectness relative to the specifics of the PICO question, inconsistency in the results, and risk of reporting bias. Observational studies, on the other hand, start off as low-level evidence but can be upgraded to moderate or even high if exceptionally large and consistent treatment effects increase confidence in the findings, especially if there is a strong dose-response gradient.

The final grades are combinations reflecting the strength of the recommendation and the quality of the evidence. Strong recommendations with high quality evidence, grade of 1A, are less common than in past editions of these guidelines, since the evidence is assessed with greater rigor for most topics, and few studies without important limitations are available.

However, recommendations that do attain this score are those for which the panel could state with confidence that new studies would be unlikely to change the direction of the effect. These recommendations apply to most patients in most circumstances. But as the grades decline, patient values and preferences likely would play an increasingly greater role in determining the best treatments or interventions for each patient.

The Final Conference

As the evidence reviews were completed and the tables and profiles prepared, the manuscripts and recommendations were drafted. Members of the article committees convened by phone or e-mail to discuss the evidence and work on drafting and grading the recommendations. These discussions generally resulted in agreement on both the quality of the evidence and strength of the recommendations.

The manuscripts and supporting tables were then reviewed by members of the Executive Committee and, after several iterations, the revised versions were shared among all panelists and the representatives of invited organizations in advance of the conference. The other panelists and representatives were asked not only to provide feedback but also to review the recommendations to identify any controversies. A recommendation was deemed to be controversial if at least one person disagreed with the wording or the grading, if there was controversy in practice, if there were wide variations in practice, or if at least one person asked that it be discussed among the broader panel and association representatives. These identified controversies composed the main agenda for the conference.

See the "Methodology for Development of Guidelines for Lung Cancer" (see the "Availability of Companion Documents" field) for more information.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation, low- or very-low-quality evidence, Grade 1C	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect
Weak	Benefits closely	Evidence from RCTs with important	Best action may differ depending on

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
recommendation, moderate-quality evidence, Grade 2B	balanced with risks and burden	limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Cost Analysis

American College of Chest Physicians (ACCP) guidelines include consideration of resources in recommendations under selected circumstances. If it is likely that resource considerations would impact the direction or strength of a recommendation, a search for cost-effectiveness studies may have been conducted. Most recommendations in these guidelines do not include a full assessment of resource considerations. However, they can be adapted to middle- and low-income countries using the ADAPTE strategies.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Peer Review

Once Executive Committee approval was received, the articles were submitted to American College of Chest Physicians (ACCP) staff for several layers of review. All reviewers were required to undergo a full conflict of interest (COI) appraisal before being approved. In the first round of reviews, the Thoracic Oncology NetWork reviewed the content of the manuscripts and the members of the Guidelines Oversight Committee (GOC) assessed the manuscripts for adherence to the methodology and conformance with the evidence. The ACCP President also appointed members of the Board of Regents to evaluate the guidelines in depth. All comments were collated into spreadsheets to ensure that they were appropriately answered. GOC and board reviewers discussed each comment and determined which should be mandatory for the authors to amend and which were provided as suggestions for improvement. All reviews and comments were anonymous, and authors were required to respond to all mandatory issues either by revising the manuscripts or providing written justification explaining why they did not agree with the reviewers' comments.

The revised manuscripts were submitted for round II review, simultaneously with the Journal peer review. Once the GOC and board reviewers approved the manuscripts, the ACCP President, President Elect, President Elect Designee, and Immediate Past President reviewed the guidelines. Approval was granted pending confirmation from the Board of Regents, before submission to the journal for final review by the Journal Editor. In addition to this extensive review process, which included nearly 30 individual reviewers from the ACCP leadership, external organizations were provided with opportunities to provide feedback before, during, and just after the conference. This final version was submitted for consideration for endorsement to all of the invited organizations, whether or not they sent representatives to the conference. However, once the guidelines were approved by the ACCP Board of Regents, no further changes were accepted. Organizations that provided endorsements are listed in each article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate treatment for patients with stage III non-small cell lung cancer (NSCLC)

Potential Harms

Concurrent chemoradiotherapy has several drawbacks, including difficulty in maintaining full-dose chemotherapy sufficient to treat systemic disease, especially with some of the newer agents such as gemcitabine, docetaxel, and paclitaxel of which all require dose reductions when given concurrently with radiotherapy. Looking at collective data from multiple phase 2 trials, acute and late toxicities associated with combined chemotherapy and radiotherapy have included mild to severe esophagitis, pneumonitis, and treatment-related death.

Contraindications

Contraindications

It is often stated that resection after neoadjuvant therapy is contraindicated if a pneumonectomy is required. Although the perioperative mortality after pneumonectomy is a significant concern, this may be a less important issue in high-volume centers with documented low mortality rates. In summary, pneumonectomy after neoadjuvant therapy probably should not be performed unless it is done in a center that has a demonstrated low mortality rate for this procedure (and the same argument holds true for lobectomy).

Qualifying Statements

Qualifying Statements

- American College of Chest Physicians (ACCP) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at the *CHEST* Web site .
- Although the ACCP is moving toward the production of evidence profiles for all guideline recommendations, there were many recommendations for which profiles were not developed, mostly because of resource constraints. When possible, methodologists created evidence profiles, and all panelists were educated on how to read and interpret them. The population, intervention, comparator, and outcome (PICO)-based systematic literature review process was followed for most recommendations, but there were some that could have benefited from meta-analyses.
- One limitation of all guidelines today is that they are not able to adequately address complex patients with multiple morbidities. This is largely because these patients are generally excluded from clinical trials and are often not included in observational studies. Since guidelines are reliant on evidence published in the peer-reviewed literature, the scientific foundation impedes the process of providing good guidance for these patients and is a limitation in these guidelines. Therefore, the ACCP encourages funding agencies to ensure that topics with limited evidence are addressed in future research.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

These guidelines are widely disseminated through the *CHEST* journal publication, National Guideline Clearinghouse, and Guidelines International

Network library. Additional clinical resources will soon be available to users of CHEST Evidence, an upcoming tool for searching the content of America College of Chest Physicians (ACCP) guidelines.

As the expanding research into diagnostic techniques and treatment options continues to evolve, the guidelines must be updated and kept current. This edition of the ACCP Lung Cancer Guidelines will be the last to be published as a complete collection, as the ACCP is now embarking on a new living guidelines model (LGM) for revising existing recommendations and developing new recommendations as the literature evolves. This will include a continual assessment of the currency of these recommendations relevant to new research studies as they are published. The review cycle for the ACCP Lung Cancer Guidelines will begin 1 year after publication unless the content experts who monitor the literature bring a recommendation or set of related recommendations to the attention of the Guideline oversight Committee (GOC), suggesting that those recommendations are in need of updating sooner. The new LGM will permit a more nimble approach to guideline development but also requires a point-of-care accessible vehicle, CHEST Evidence, for the users to readily search for the most current version. These features will be described in greater detail in upcoming publications. As a step in this direction, these guidelines will be published primarily online with a printed version of the Executive Summary, containing all of the recommendations, the introduction, and this article on methodology. All narratives for each article with their supporting tables, figures, and algorithms will be available online at journal.publications.chestnet.org.

Implementation Tools

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Ramnath N, Dilling TJ, Harris LJ, Kim AW, Michaud GC, Balekian AA, Diekemper R, Detterbeck FC, Arenberg DA. Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e314S-40S. [132 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Jan (revised 2013 May)

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

- The development of this guideline was supported primarily by the American College of Chest Physicians (ACCP). The lung cancer guidelines conference was supported in part by a grant from the Lung Cancer Research Foundation. The publication and dissemination of the guidelines was supported in part by a 2009 independent educational grant from Boehringer Ingelheim Pharmaceuticals, Inc.
- Role of sponsors: The ACCP was solely responsible for the development of these guidelines. The remaining supporters played no role in the development process. External supporting organizations cannot recommend panelists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Further details on the Conflict of Interest (COI) Policy are available online at http://chestnet.org .
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the source of funding for this guideline.

Guideline Committee

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

Composition of Group That Authored the Guideline

Authors: Nithya Ramnath, MD; Thomas J. Dilling, MD; Loren J. Harris, MD, FCCP; Anthony W. Kim, MD, FCCP; Gaetane C. Michaud, MD, FCCP; Alex A. Balekian, MD, MSHS; Rebecca Diekemper, MPH; Frank C. Detterbeck, MD, FCCP; Douglas A. Arenberg, MD, FCCP

Financial Disclosures/Conflicts of Interest

- Conflicts of Interest (COI) grids reflecting the conflicts of interest that were current as of the date of the conference and voting are posted in the online supplementary materials.
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- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the conflict of interest procedures and requirements for the guideline panel.

Guideline Endorser(s)

American Association for Bronchology and Interventional Pulmonology - Medical Specialty Society

European Society of Thoracic Surgeons - Professional Association

Oncology Nursing Society - Professional Association

Society of Thoracic Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Robinson LA, Ruckdeschel JC, Wagner H Jr, Stevens CW, American College of Chest Physicians. Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):243S-65S.

Jett JR, Schild SE, Keith RL, Kesler KA, American College of Chest Physicians. Treatment of non-small cell lung cancer, stage IIIB: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):266S-76S.

Guideline Availability

Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal. Also available to Chest subscribers through the Chest app for iPhone and iPad.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

Availability of Companion Documents

The following are available:

- Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Supporting data. Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.
- Detterbeck FC, Zelman Lewis S, Diekemper R, Addrizzo-Harris D, Alberts MW. Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Executive summary. Chest 2013 May;143(5 Suppl):7S-37S. Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.
- Alberts WM. Introduction to the third edition: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):38S-40S. Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.
- Zelman Lewis S, Diekemper R, Addrizzo-Harris DJ. Methodology for development of guidelines for lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):41S-e50S. Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.
- Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e1S-e29S. Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.
- Nana-Sinkham SP, Powell CA. Molecular biology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e30S-e39S. Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.
- Detterbeck FC, Postmus PE, Tanoue LT. The stage classification of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e191S-e210S. Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL

60062-2348.

The following is also available:

- Highlights of the ACCP diagnosis and management of lung cancer guidelines, 3rd ed. Podcast. Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site .

A lung cancer staging calculator is available from the Staging Lung Cancer Web site .

Patient Resources

The following are available:

- Lung cancer: understanding the diagnosis. Northbrook (IL): American College of Chest Physicians; 2010. 7 p. Electronic copies: Available in Portable Document Format (PDF) from the OneBreath.org Web site .
- Understanding non-small cell lung cancer. A guide for the patient. Northbrook (IL): American College of Chest Physicians; 2010. 3 p. Electronic copies: Available in PDF from the OneBreath.org Web site .

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